Annals of Pharmacotherapy

Potentially Inappropriate Prescribing in Older Patients Discharged from Acute Care Hospitals to Residential Aged Care Facilities

Journal:	*The Annals of Pharmacotherapy*
Manuscript ID:	AOP-14-0326
Manuscript Type:	Research Report (Original research/clinical trials)
Keywords:	Drug Safety, Geriatrics, Medication safety, Palliative care, Aging

Abstract:

Background: The frequency of prescribing potentially inappropriate medications (PIMs) in older patients remains high despite evidence of adverse outcomes from their use. Little is known about whether admission to hospital has any effect on appropriateness of prescribing.

Objectives: This study aimed to identify the prevalence and nature of PIMs and explore the association of risk factors for receiving a PIM.

Methods: This was a prospective study of 206 patients discharged to residential aged care facilities (RACFs) from acute care. All patients were aged at least 70 years and were admitted between July 2005 and May 2010; their admission and discharge medications were evaluated.

Results: Mean patient age was 84.8 ± 6.7 years; the majority (57%) were older than 85 years and mean (SD) Frailty Index was 0.42 (0.15). At least one PIM was identified in 112 (54.4%) patients on admission and 102 (49.5%) patients on discharge. Of all medications prescribed at admission (1728), 10.8% were PIMs and at discharge of 1759 medications, 9.6% were PIMs. Of total 187 PIMs on admission, 56 (30%) were stopped and 131 were continued; 32 new PIMs were introduced. Of the potential risk factors considered, in-hospital cognitive decline and frailty status were the only significant predictors of PIMs.

Conclusion: Although, admission to hospital is an opportunity to review the indications for specific medications, a high prevalence of inappropriate drug use was observed. The only associations with PIM use were the frailty status and in-hospital cognitive decline. Additional studies are needed to further evaluate this association.

Keywords: Beers criteria, frailty, inappropriate prescribing, older patients, residential aged care facilities

Potentially Inappropriate Prescribing in Older Patients Discharged from Acute Care Hospitals to Residential Aged Care Facilities

A Poudel[1], NM Peel[2], L Nissen[3], C Mitchell[4], LC Gray[5], RE Hubbard[6]

1. PhD Scholar, School of Pharmacy, The University of Queensland, Brisbane, QLD, Australia.
2. Senior Research Fellow, Centre for Research in Geriatrics Medicine, The University of Queensland, Brisbane, QLD, Australia.
3. Professor, School of Clinical Sciences, Queensland University of Technology, School of Pharmacy, The University of Queensland , Centre for Safe and Effective Prescribing, The University of Queensland, Brisbane, QLD, Australia.
4. Associate Professor, Centre for Safe and Effective Prescribing, The University of Queensland, Brisbane, QLD, Australia.
5. Professor, Centre for Research in Geriatrics Medicine, The University of Queensland, Brisbane, QLD, Australia
6. Senior Lecturer, Centre for Research in Geriatrics Medicine, The University of Queensland, Brisbane, QLD, Australia

Corresponding author

Arjun Poudel
School of Pharmacy
The University of Queensland
20 Cornwall Street, Woolloongabba, QLD 4102
Ph: +61416503006 Email: a.poudel@uq.edu.au

Presentation of abstract/poster: Abstract presented as a poster in Annual Scientific Meeting of the American Geriatrics Society, Orlando, FL. May 15-17, 2014.
Word count: Text 2842; Abstract 250
Number of refs: 48 **Tables:** 4

ABSTRACT

Background: The frequency of prescribing potentially inappropriate medications (PIMs) in older patients remains high despite evidence of adverse outcomes from their use. Little is known about whether admission to hospital has any effect on appropriateness of prescribing.

Objectives: This study aimed to identify the prevalence and nature of PIMs and explore the association of risk factors for receiving a PIM.

Methods: This was a prospective study of 206 patients discharged to residential aged care facilities (RACFs) from acute care. All patients were aged at least 70 years and were admitted between July 2005 and May 2010; their admission and discharge medications were evaluated.

Results: Mean patient age was 84.8 ± 6.7 years; the majority (57%) were older than 85 years and mean (SD) Frailty Index was 0.42 (0.15). At least one PIM was identified in 112 (54.4%) patients on admission and 102 (49.5%) patients on discharge. Of all medications prescribed at admission (1728), 10.8% were PIMs and at discharge of 1759 medications, 9.6% were PIMs. Of total 187 PIMs on admission, 56 (30%) were stopped and 131 were continued; 32 new PIMs were introduced. Of the potential risk factors considered, in-hospital cognitive decline and frailty status were the only significant predictors of PIMs.

Conclusion: Although, admission to hospital is an opportunity to review the indications for specific medications, a high prevalence of inappropriate drug use was observed. The only associations with PIM use were the frailty status and in-hospital cognitive decline. Additional studies are needed to further evaluate this association.

Keywords: Beers criteria, frailty, inappropriate prescribing, older patients, residential aged care facilities

Introduction

Our aging population, while a consequence of societal success, does present a challenge to the health care system. Older people are prescribed multiple medications and are more prone to adverse drug events (ADEs) that lead to increased mortality and morbidity and higher health care cost.[1-3] The appropriate use of available pharmacotherapy requires consideration of both the benefits and risks of the medications. Drugs are classified as potentially inappropriate when the risks of treatment outweigh the benefits[4]; they are prescribed for longer periods than clinically indicated or without any clear indication; they are not prescribed when indicated[5]; and when they are likely to interact with other drugs and diseases.[6]

Inappropriate prescribing in older patients can be detected using either explicit (criterion-based) or implicit (judgment-based) screening tools.[7-9] Explicit criteria are derived from expert reports or published reviews. They have high reliability and reproducibility but focus mainly on specific drugs and disease states. By contrast, implicit criteria are person-specific and explore patient preferences, rather than the disease and medications; they rely on evaluator judgment and tend to have low reliability and poor clinical utility.[10] Although these criteria address some aspects of prescribing in older patients, they seldom consider the frailty of such patients. The omission of health status from established prescribing tools may help to explain the lack of clinical benefit from algorithm-based medication reviews.[3] The Beers criteria are commonly used and they do measure some surrogates of frailty. They were originally developed in 1991 [11] for use in the older nursing home population and have been subsequently updated in 1997, 2002 and 2012 so as to be applicable to all persons over 65 years of age, regardless of their place of residence.[12-14] The recently updated Beers criteria divide medications into three main categories according to major therapeutic classes and

organ systems: 34 medications are considered potentially inappropriate, independent of diagnosis, 14 are to be avoided in older adults with certain diseases and syndromes that can be exacerbated by the listed drug , while another 14 are to be used with caution in older adults.[14] Although many medications on the Beers list are not available in Australia, use of these criteria for evaluation of prescribing has the advantage of enabling international comparison.

Admission to hospital is an opportune time to review and rationalize prescribing, weighing up the benefits of pharmacotherapy against significant risks of polypharmacy and inappropriate prescribing in older adults, particularly those who are frail. However, little is known about whether admission to hospital has any effect on appropriateness of prescribing. Potentially inappropriate prescribing (PIP) is particularly common in long-term residents of aged care facilities; indeed institutionalization itself is an established independent risk factor for PIP.[15] Studies that have compared prevalence of potentially inappropriate medications (PIMs) at admission to hospital and discharge have reported inconsistent results. A prospective drug surveillance in an acute medical geriatric unit in France reported a decreased prevalence of PIMs from 66% at admission to 43.6% at discharge.[16] A retrospective, non-randomised study in the Specialist Health and Ageing Unit in England, UK found a decreased prevalence from 26.7% at admission to 22.6% at discharge.[17] By contrast a similar study in Norway showed the increased prevalence of PIMs from 24% at admission to 35% at discharge.[18]

Similar reports from Australian health care settings are limited and we cannot assume identical prevalence rates and PIM types in Australia due to the variations in health care systems and prescribing practices across countries. Therefore the main objective of this study was to determine the prevalence of PIP using the 2012 version of the American Geriatrics

Society (AGS) Beers Criteria in patients discharged from acute care to residential aged care facilities (RACFs). We also aimed to identify whether polypharmacy, age, gender, in-hospital falls, delirium, functional and cognitive decline and the frailty status of patients were independent risk factors for receiving an inappropriate medication.

Methods

Study population: This is a prospective study of patients, aged 70 and older, who were discharged to RACFs (206 out of total 1418 patients) following admission to 11 acute care hospitals in Queensland and Victoria, Australia. The sites ranged from small secondary care centres (with 120 – 160 beds, n = 2), through rural hospitals (250 – 280 beds, n = 2) to metropolitan teaching facilities (300 – 450 beds, n = 4) and major tertiary referral centres (>650 beds; n = 3). All patients were admitted to the acute care hospitals between July 2005 and May 2010. Patient recruitment has been described in detail elsewhere.[19, 20] Patients were excluded if they were admitted to coronary or intensive care units, for terminal care only or were discharged from hospital within 24 hours. Only those patients entering RACFs at discharge were included in the study.

Data collection and measurement tools: The interRAI Acute Care assessment tool was used for data collection.[21] It has been specifically developed for use in the acute setting, to support Comprehensive Geriatric Assessment (CGA) for older inpatients.[22, 23] This instrument screens a large number of domains around socio-demographic information, physical, cognitive and psycho-social functioning, medications, medical diagnoses, advance directives, and discharge destination.[23] Trained nurse assessors gathered data at admission (within 24 hours in the ward) and at discharge. A number of scales are embedded within the interRAI instruments combine single items belonging to domains such as activities of daily living (ADL),

instrumental activities of daily living (IADL) and cognition, which are used to describe the presence and extent of deficits in these domains.[22] For each patient, all prescribed medication, including Anatomical Therapeutic Classification (ATC) codes, was recorded on admission and at discharge. Data were entered by pharmacists or pharmacy students and verified by a second pharmacist or geriatrician.

Deriving a Frailty Index: A Frailty index (FI), an index of accumulated deficits, was calculated for each individual at admission using a well-defined methodology.[24] Data collected using the interRAI assessment tool was coded as deficits. For example, in the domain of cognition, an acute change in mental status is recorded as a dichotomous, yes/ no response and this was coded as deficit present (1 point) or absent (0 points). Other data were recorded on an ordinal scale with cut-offs for 0/ 0.5/1 deficit coded according to the distribution of the data. For example, the domain of vision classified into four categories (0: adequate, 1: minimal difficulty, 2: moderate difficulty, 3: severe difficulty, 4: no vision) is coded with cut-offs of 0/0.5/1 (i.e. 0 = 0, 1 = 0.5, 2-4 = 1).Deficits crossed the domains of function, cognition, mood and behaviour, disease diagnoses and sensory impairments. Medication use was excluded from the FI. Each individual's deficit points were then summed and divided by the total number of deficits considered (here, 52). For example, someone with 6 deficits out of 40 counted has a FI of 0.15. The FI has a potential score of 0-1, where 0= absence of all deficits, and 1= all deficits present.[25] Although the FI can be considered as a continuous variable with higher values representing greater frailty, 0.25 has been proposed as the cut-off between 'fit' and 'frail' individuals.[26]

Polypharmacy: Polypharmacy was categorised into three groups based on the number of drugs in use. Hyper polypharmacy was defined as concurrent use of ten or more drugs;

polypharmacy was defined as use of five to nine drugs and non-polypharmacy represented patients using four or less drugs concomitantly. These cut-off points have been selected based on previous studies relating the risk of adverse outcomes in older people to numbers of prescribed medication.[27, 28]

Covariates

Fall in hospital: In-hospital fall was defined as having at least one fall during the period of hospitalization. These data were collected prospectively by daily chartreviews and ward visits by the research nurses using allavailable sources of information (interviewing the patientand medical staff, reviewing the medical records, andchecking the forms or systems for recording adverseevents).[29] The process of data collection was based on thedetailed instructions provided in the tool manual.[21]

Delirium in hospital: As part of the interRAI AC, varying mental function and acute changes in mental status from baseline was assessed by nurse assessor at admission and discharge. The two items were combined to screen for delirium. [30] Delirium in hospital was recorded if delirium screened positive at the admission or discharge assessments or if noted in the hospital records on daily ward visits by the nurse assessor.

Failure to improve in ADL: Failure in improvement of ADL was assessed using change in the ADL short form scale that consists of four items (personal hygiene, walking, toilet use, and eating). Scores on the ADL scale range from 0 to 16, with higher scores indicating greater impairment.[20] Failure to improve in ADL was defined as those with some ADL impairment on admission who had the same or worse (higher) ADL score on discharge compared to admission or who developed a new ADL impairment in hospital.

In-hospital cognitive function decline: The Cognitive Performance Scale (CPS) was used to measure cognitive impairment.[20] Score ranges from '0' to '6'with higher scores indicating greater impairment. In-hospital cognitive decline was defined as having a worse CPS score on discharge compared to admission.

Statistical analysis: Data were analysed using the Statistical Package for the Social Sciences 21.0 (IBM SPSS Statistics 21.Ink). A paired sample t-test was used to observe the relationship between admission and discharge medications. Standard multiple regression was used to detect risk factors for PIMs at both admission and discharge. Age, gender, number of admission and discharge medications, in-hospital falls, delirium, functional and cognitive decline and frailty index of patients were used as predictive variables for PIMs. A p-value of 0.05 was considered statistically significant.

Ethics: Ethics approval was obtained from the human research and ethics committee of each participating hospitals and The University of Queensland Medical Research Ethics Committee. All patients or their substitute decision-maker gave informed consent for participation.

Results

Patient characteristics: Of the 206 patients discharged to RACFs, 142 (69%) were female. The principal characteristics of the study population are described in Table 1. They had a mean (SD) age of 84.8 (6.8) years; the majority (57%) were older than 85 years and mean (SD) Frailty Index was 0.42 (0.15).A total of 35%were admitted from the community and 65% from RACFs. The median length of stay in hospital was eight days. Of those discharged

to RACFs, approximately 60% were discharged to high care (a high level care setting for older people with 24-hour nursing care) and remaining 40% discharged to low care (residents require accommodation and personal care type services, but not 24-hour nursing care).

General prescribing pattern: The number of medications prescribed on admission and discharge is shown in Table 2. Patients were prescribed a mean of 7.2 (±3.81) regular medications at admission and 8.1 (±3.95) on discharge to RACF. Comparing medication regimes at admission and discharge, the prevalence of polypharmacy was stable [106 (51.5%) vs 102 (49.5%) respectively] but with an increase in hyper-polypharmacy [from 50 patients (24.3%) to 67 (32.5%)].

At admission, two patients were prescribed 23 medications with 10 patients receiving at least 20 medications. On discharge one (different to admission) patient was prescribed 23 medications and four patients had at least 20 medications.At discharge, aspirin and anti-platelet agents were the most frequently prescribed medications (109, 54%), followed by anti-ulcer drugs in 105 (52%) patients. Other prevalent medication included antidepressants (28.2%), benzodiazepines (19.3%), antipsychotics (16.3%) and opioids (16.3%). Of the potential risk factors, frailty status and in-hospital cognitive decline were the only significant predictors of PIMs at both admission (p= 0.047) and discharge (p = 0.032). However, no association was observed between PIM use, polypharmacy categories, age, gender, in-hospital falls, delirium and functional decline.

Potentially inappropriate medications at admission: On admission, 112 (54%) patients were on at least one PIM; 5 patients were on 4 PIMs. Of the 1460 regular medications prescribed at admission 187 (12.8%) were PIMs. Of these, 149 (80%) were classified as PIMs for older

people independent of diagnosis and 38 (20%) PIMs contraindicated in older people with certain diseases or syndromes (Table 3). PIMs to be used with caution accounted for 3.8% of total medications prescribed. Commonly prescribed PIM categories were central nervous, cardiovascular and gastrointestinal system drugs, and analgesics. Multiple regression analysis revealed that frailty status was significantly associated to PIMs at admission [($p<0.05$ OR= -1.01 (-2.01, -0.01)]. Age, gender and number of admission medications were not associated with being prescribed PIMs.

Potentially inappropriate medications at discharge: At discharge, 102 (49.5%) patients were on at least one PIM; one patient was discharged on 7 PIMs, 5 patients on 4 PIMs and 8 patients on 3. Of all the 1652 regular medications prescribed at discharge, 168 (10.1%) were PIMs. Of these 168, 129 (77%) were classified as PIMs for older people independent of diagnosis and 39 (23%) of PIMs contraindicated in older people with certain diseases or syndromes (Table 3). PIMs to be used with caution accounted for 3.7% of total medications prescribed. Commonly prescribed PIMs categories were Central Nervous system (CNS) drugs, cardiovascular, gastrointestinal, respiratory medications, analgesics and antimuscarinics. Multiple regression analysis showed that only frailty status was a predictor of the number of PIMs at discharge [($p<0.05$, OR= -2.15, -0.10)].

Changes in potentially inappropriate medication between admission and discharge: Table 4 shows the number of patients with total PIMs at admission and discharge. Of the 187 PIMs prescribed at admission, 56 (30%) were stopped and 131 (70%) were continued while 32 new PIMs were started. PIMs introduced included CNS drugs [benzodiazepines (14/32), antipsychotics (8/32), and antidepressants (1/32)], respiratory medications (3/32), antiarrhythmics (2/32), gastrointestinal (2/32) and analgesics (2/32).

Discussion

The present study demonstrated frequent use of inappropriate medications in older people discharged from acute care hospitals to RACFs. 54.4% of patients were on at least one PIM at admission to hospital with a non-significant trend to fewer PIMs on discharge (49.5%). The frailty status of patients and in-hospital cognitive decline were the only significant predictors for receiving PIMs at both admission and discharge. To our knowledge, this is the first study to identify this association.

The prevalence of PIMs observed in this study population differ from those of previous studies using the recent updated 2012 Beers criteria. A higher prevalence (82.6%) was observed in a Brazilian long term care home study [31] and around 66% was observed in an Argentinian geriatric hospital.[32] Yet a very low prevalence (16% and 25.5%) was noticed in tertiary health care setting in India and Nigeria respectively.[33, 34] Commonly prescribed PIM categories at both admission and discharge were CNS, cardiovascular, gastrointestinal and respiratory drugs, and analgesics which are similar to those reported in other studies.[35-38] Of note, 30% of PIMs were stopped and other new PIMs were introduced at discharge. We found a clear association between the use of PIMs, frailty status and cognitive decline of patients at admission and discharge. However, no association was observed between PIM use, age and gender, which is consistent with previous reports.[39, 40] Also, no association of PIM use with in-hospital falls, delirium and functional decline was observed. Furthermore, in contrast to other studies, [41-44] we found no association between polypharmacy and PIM use.

There are a number of limitations to this study. Although patients were recruited from multiple hospital sites, the sample size is relatively small .The recently updated Beers criteria contain medications which are either not available in Australia (e.g. carisoprodol and

trimethobenzamide) or which have been withdrawn from use here (chlorpropamide, reserpine and phenylbutazone). Thus, the relevance of the tool within Australia could be questioned.[5] Moreover, these criteria also fail to address other issues such as drug duplication, under-prescribing, and drug-drug interaction.[14, 45-47] Hence, the prevalence of PIMs may be higher than those reported in this study. However, this study demonstrated the prevalence of PIMs in frail older patients on admission and discharge and adds to existing research by identifying patient's frailty status as a unique risk factor associated with the use of PIMs.

These discrepancies in Beers and other established criteria should be addressed either by developing new criteria or by refining the existing tools to make them more applicable to frail older people. The first and foremost step is to identify the frail patient in clinical practice by applying clinically validated tools (e.g. frailty index). Once the frail patient has been identified, there is a need for specific measures or criteria to assess appropriateness of therapy that consider such factors as quality of life, functional status and remaining life expectancy and thus modified goals of care.[48]

Conclusion

A high prevalence of potentially inappropriate drug prescribing was observed in older patients on admission to acute care hospitals and on discharge to RACFs. Frailty status and in-hospital cognitive decline of patients were risk factors for the use of PIMs. The findings of this study provide a basis for designing interventions to rationalize prescribing in older patients. Further studies in different settings with larger population are warranted to evaluate the prevalence of potentially inappropriate medications and deviations in prescribing practices.

Acknowledgements

No sources of funding were used to conduct this study. The authors have no conflicts of interest that are directly relevant to the content of this study.

Table 1: Characteristics of study population

Characteristics	Value
Age distribution	
Mean age [SD]	84.8 [6.8]
65-74 years	20 [10]
75-84 years	69 [33]
>85 years	117 [57]
Sex (n [%])	
Female	142 [69]
Male	64 [31]
Admitted from (n [%])	
Community	73 [35.4]
RACF low care	64 [31.1]
RACF high care	69 [33.5]
Discharged to(n [%])	
RACF low care	81 [39.3]
RACF high care	125 [60.7]
Length of stay (days)	
Median length of stay (days [IQR])	8 [4-16]
Frailty Index	
Mean (SD)	0.42 (0.15)

IQR: Interquartile range

Table 2: Number of regular medications prescribed on admission and discharge

Medication category	Admission N [%]	Discharge N [%]
Mean (SD)	7.2 [3.81]	8.1 [3.95]
0 - 4 medications (non-polypharmacy)	47 [22.8]	35 [17.0]
5-9 medications (polpharmacy)	106 [51.5]	102 [49.5]
≥10 medications (excessive polypharmacy)	50 [24.3]	67 [32.5]
Missing	3 [1.5]	2 [1.0]
Total	**1460**	**1652**

Table 3: Potentially inappropriate medications (PIMs) on admission and discharge as determined by Beers criteria

PIMs independent of medical condition					**PIMs in the presence of certain pathologies**					**PIMs to be used with caution**				
	Admission		**Discharge**			**Admission**		**Discharge**			**Admission**		**Discharge**	
System/therapeutic category/drugs	**N**	**%**	**N**	**%**	**System/therapeutic category/drugs**	N	%	N	%	**System/therapeutic category/drugs**	N	%	N	%
Central Nervous System	**106**	**71.1**	**102**	**79**	**Central Nervous System**	**11**	**29.9**	**10**	**25.6**	**Antipsychotics**	**14**	**25.5**	**15**	**24.6**
Antidepressants	9	6	8	6.2	Antidepressants	2	5.3	2	5.1	**SNRIs**	**3**	**5.5**	**4**	**6.5**
Antipsychotics	50	33.6	40	31	Antipsychotics	9	23.7	8	20.5	**SSRIs**	**31**	**56.3**	**35**	**57.4**
Cardiovascular	**47**	**31.5**	**54**	**41.8**	**Cardiovascular**	**12**	**31.5**	**9**	**23**	**TCAs**	**7**	**12.7**	**7**	**11.5**
Alpha blockers	4	2.7	4	3.1	**Gastrointestinal**	**8**	**21**	**10**	**25.6**					
Antiarrhythmic	14	9.4	7	5.4	**Respiratory**	**5**	**13.1**	**8**	**20.5**					
Gastrointestinal	**23**	**15.5**	**12**	**9.3**	**Antimuscarinics**	**2**	**5.2**	**2**	**5.1**					
Analgesics	**2**	**1.4**	**4**	**3.1**										
Total	**149**	**100**	**129**	**100**		**38**	**100**	**39**	**100**		**55**	**100**	**61**	**100**

TCAs (Tricyclic antidepressants): SSRIs (Selective Serotonin Reuptake Inhibitors): SNRIs (Selective Norepinephrine Reuptake Inhibitors)

Table 4: Potentially inappropriate medication distribution at admission and discharge

Number of PIMs	**Number of patients (%)** **n= 206**	
	Admission	**Discharge**
No PIMs	94 (45.6)	104 (50.5)
One PIM	60 (29.1)	59 (28.6)
Two PIMs	34 (16.5)	29 (14.1)
Three PIMs	13 (6.3)	8 (3.9)
Four or more PIMs	5 (2.4)	6 (2.9)
Total number of patients with at least one PIM	**112 (54.4)**	**102 (49.5)**

References

1. Hubbard RE, O'Mahony MS, Woodhouse KW. Medication prescribing in frail older people. Eur J Clin Pharmacol. 2013;69(3):319-26. doi:10.1007/s00228-012-1387-2.

2. McLachlan AJ, Bath S, Naganathan V et al. Clinical pharmacology of analgesic medicines in older people: impact of frailty and cognitive impairment. Br J Clin Pharmacol. 2011;71(3):351-64. doi:10.1111/j.1365-2125.2010.03847.x.

3. Poudel A, Hubbard RE, Nissen L, Mitchell C. Frailty: a key indicator to minimize inappropriate medication in older people. QJM. 2013;106(10):969-75. doi:10.1093/qjmed/hct146.

4. O'Mahony D, Gallagher PF. Inappropriate prescribing in the older population: need for new criteria. Age Ageing. 2008;37(2):138-41. doi:10.1093/ageing/afm189.

5. Wahab MS, Nyfort-Hansen K, Kowalski SR. Inappropriate prescribing in hospitalised Australian elderly as determined by the STOPP criteria. Int J Clin Pharm. 2012:aheadofprint. doi:10.1007/s11096-012-9681-8.

6. Hanlon JT, Schmader KE, Ruby CM, Weinberger M. Suboptimal prescribing in older inpatients and outpatients. J Am Geriatr Soc. 2001;49(2):200-9.

7. Dimitrow MS, Airaksinen MS, Kivela SL, Lyles A, Leikola SN. Comparison of prescribing criteria to evaluate the appropriateness of drug treatment in individuals aged 65 and older: a systematic review. J Am Geriatr Soc. 2011;59(8):1521-30. doi:10.1111/j.1532-5415.2011.03497.x.

8. Levy HB, Marcus EL, Christen C. Beyond the beers criteria: A comparative overview of explicit criteria. Ann Pharmacother. 2010;44(12):1968-75.

9. Luo R, Scullin C, Mullan AM, Scott MG, McElnay JC. Comparison of tools for the assessment of inappropriate prescribing in hospitalized older people. J Eval Clin Pract. 2012;18(6):1196-202. doi:10.1111/j.1365-2753.2011.01758.x.

10. Gnjidic D, Hilmer SN. Use of potentially inappropriate medications in the care of frail older people. Aging Health. 2010;6(6):705-16.

11. Beers MH, Ouslander JG, Rollingher I, Reuben DB, Brooks J, Beck JC. Explicit criteria for determining inappropriate medication use in nursing home residents. UCLA Division of Geriatric Medicine. Arch Intern Med. 1991;151(9):1825-32.

12. Beers MH. Explicit criteria for determining potentially inappropriate medication use by the elderly. An update. Arch Intern Med. 1997;157(14):1531-6.

13. Fick DM, Cooper JW, Wade WE, Waller JL, Maclean JR, Beers MH. Updating the Beers criteria for potentially inappropriate medication use in older adults: results of a US consensus panel of experts. Arch Intern Med. 2003;163(22):2716-24. doi:10.1001/archinte.163.22.2716.

14. Campanelli CM. American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2012;60(4):616-31. doi:10.1111/j.1532-5415.2012.03923.x.

15. Haasum Y, Fastbom J, Johnell K. Institutionalization as a risk factor for inappropriate drug use in the elderly: a Swedish nationwide register-based study. Ann Pharmacother. 2012;46(3):339-46. doi:10.1345/aph.1Q597.

16. Laroche ML, Charmes JP, Nouaille Y, Fourrier A, Merle L. Impact of hospitalisation in an acute medical geriatric unit on potentially inappropriate medication use. Drugs Aging. 2006;23(1):49-59.

17. Onatade R, Auyeung V, Scutt G, Fernando J. Potentially inappropriate prescribing in patients on admission and discharge from an older peoples' unit of an acute UK hospital. Drugs Aging. 2013;30(9):729-37. doi:10.1007/s40266-013-0097-5.

18. Bakken MS, Ranhoff AH, Engeland A, Ruths S. Inappropriate prescribing for older people admitted to an intermediate-care nursing home unit and hospital wards. Scand J Prim Health Care. 2012;30(3):169-75. doi:10.3109/02813432.2012.704813.

19. Brand CA, Martin-Khan M, Wright O et al. Development of quality indicators for monitoring outcomes of frail elderly hospitalised in acute care health settings: study protocol. BMC health services research. 2011;11:281. doi:10.1186/1472-6963-11-281.

20. Lakhan P, Jones M, Wilson A, Courtney M, Hirdes J, Gray LC. A prospective cohort study of geriatric syndromes among older medical patients admitted to acute care hospitals. Journal of the American Geriatrics Society. 2011;59(11):2001-8. doi:10.1111/j.1532-5415.2011.03663.x.

21. Gray LC, Arino-Blasco S, Berg K et al. interRAI Acute Care (AC) Assessment Form and User's Manual. Washington, DC: interRAI; 2010.

22. Gray LC, Berg K, Fries BE et al. Sharing clinical information across care settings: the birth of an integrated assessment system. BMC Health Serv Res. 2009;9:71. doi:10.1186/1472-6963-9-71.

23. Gray LC, Bernabei R, Berg K et al. Standardizing assessment of elderly people in acute care: the interRAI Acute Care instrument. Journal of the American Geriatrics Society. 2008;56(3):536-41. doi:10.1111/j.1532-5415.2007.01590.x.

24. Searle SD, Mitnitski A, Gahbauer EA, Gill TM, Rockwood K. A standard procedure for creating a frailty index. BMC Geriatr. 2008;8:24. doi:10.1186/1471-2318-8-24.

25. Rockwood K, Mitnitski A. Frailty in relation to the accumulation of deficits. J Gerontol A Biol Sci Med Sci. 2007;62(7):722-7.

26. Rockwood K, Andrew M, Mitnitski A. A comparison of two approaches to measuring frailty in elderly people. J Gerontol A Biol Sci Med Sci. 2007;62(7):738-43.

27. Jyrkka J, Enlund H, Korhonen MJ, Sulkava R, Hartikainen S. Polypharmacy status as an indicator of mortality in an elderly population. Drugs Aging. 2009;26(12):1039-48. doi:10.2165/11319530-000000000-00000.

28. Kuijpers MA, van Marum RJ, Egberts AC, Jansen PA. Relationship between polypharmacy and underprescribing. Br J Clin Pharmacol. 2008;65(1):130-3. doi:10.1111/j.0306-5251.2007.02961.x.

29. Ballokova A, Peel NM, Fialova D, Scott IA, Gray LC, Hubbard RE. Use of Benzodiazepines and Association with Falls in Older People Admitted to Hospital: A Prospective Cohort Study. Drugs & aging. 2014. doi:10.1007/s40266-014-0159-3.

30. Salih SA, Paul S, Klein K, Lakhan P, Gray L. Screening for delirium within the interRAI acute care assessment system. The journal of nutrition, health & aging. 2012;16(8):695-700. doi:10.1007/s12603-012-0074-4.

31. Vieira de Lima TJ, Garbin CA, Garbin AJ, Sumida DH, Saliba O. Potentially inappropriate medications used by the elderly: prevalence and risk factors in Brazilian care homes. BMC Geriatr. 2013;13:52. doi:10.1186/1471-2318-13-52.

32. Marzi MM, Diruscio AV, Nunez HM, Pires SM, Quaglia BN. Analysis of medication prescription in an Argentinian geriatric hospital. Rev Med Chil. 2013;141(2):194-201. doi:10.4067/s0034-98872013000200008.

33. Undela K, Bansal D, D'Cruz S, Sachdev A, Tiwari P. Prevalence and determinants of use of potentially inappropriate medications in elderly inpatients: A prospective study in a tertiary healthcare setting. Geriatr Gerontol Int. 2013. doi:10.1111/ggi.12081.

34. Fadare JO, Agboola SM, Opeke OA, Alabi RA. Prescription pattern and prevalence of potentially inappropriate medications among elderly patients in a Nigerian rural tertiary hospital. Ther Clin Risk Manag. 2013;6:115-20. doi:10.2147/tcrm.s40120.

35. Gallagher P, Lang PO, Cherubini A et al. Errasquin B et al. Prevalence of potentially inappropriate prescribing in an acutely ill population of older patients admitted to six European hospitals. Eur J Clin Pharmacol. 2011;67(11):1175-88. doi:10.1007/s00228-011-1061-0.

36. Hamilton H, Gallagher P, Ryan C, Byrne S, O'Mahony D. Potentially inappropriate medications defined by STOPP criteria and the risk of adverse drug events in older hospitalized patients. Arch Intern Med. 2011;171(11):1013-9.

37. Stafford AC, Alswayan MS, Tenni PC. Inappropriate prescribing in older residents of Australian care homes. J Clin Pharm Ther. 2011;36(1):33-44. doi:10.1111/j.1365-2710.2009.01151.x.

38. Hanlon JT, Artz MB, Pieper CF et al. Inappropriate medication use among frail elderly inpatients. Ann Pharmacother. 2004;38(1):9-14. doi:10.1345/aph.1D313.

39. Wawruch M, Fialova D, Zikavska M et al. Factors influencing the use of potentially inappropriate medication in older patients in Slovakia. J Clin Pharm Ther. 2008;33(4):381-92. doi:10.1111/j.1365-2710.2008.00929.x.

40. Ruggiero C, Dell'Aquila G, Gasperini B et al. Potentially inappropriate drug prescriptions and risk of hospitalization among older, Italian, nursing home residents: the ULISSE project. Drugs Aging. 2010;27(9):747-58. doi:10.2165/11538240-000000000-00000.

41. Chen LL, Tangiisuran B, Shafie AA, Hassali MA. Evaluation of potentially inappropriate medications among older residents of Malaysian nursing homes. Int J Clin Pharm. 2012;34(4):596-603. doi:10.1007/s11096-012-9651-1.

42. Hosia-Randell HM, Muurinen SM, Pitkala KH. Exposure to potentially inappropriate drugs and drug-drug interactions in elderly nursing home residents in Helsinki, Finland: a cross-sectional study. Drugs Aging. 2008;25(8):683-92.

43. Akazawa M, Imai H, Igarashi A, Tsutani K. Potentially inappropriate medication use in elderly Japanese patients. Am J Geriatr Pharmacother. 2010;8(2):146-60. doi:10.1016/j.amjopharm.2010.03.005.

44. Bao Y, Shao H, Bishop TF, Schackman BR, Bruce ML. Inappropriate medication in a national sample of US elderly patients receiving home health care. J Gen Intern Med. 2012;27(3):304-10. doi:10.1007/s11606-011-1905-4.

45. Laroche ML, Charmes JP, Bouthier F, Merle L. Inappropriate medications in the elderly. Clin Pharmacol Ther. 2009;85(1):94-7. doi:10.1038/clpt.2008.214.

46. Gallagher P, O'Mahony D. STOPP (Screening Tool of Older Persons' potentially inappropriate Prescriptions): Application to acutely ill elderly patients and comparison with Beers' criteria. Age Ageing. 2008;37(6):673-9.

47. Gallagher PF, Barry PJ, Ryan C, Hartigan I, O'Mahony D. Inappropriate prescribing in an acutely ill population of elderly patients as determined by Beers' Criteria. Age Ageing. 2008;37(1):96-101. doi:10.1093/ageing/afm116.

48. Poudel. A, Hubbard RE, Nissen. A, C M. Are prescribing indicators essentially representing the frail older population? J Frailty Aging. 2013;2(2):199.